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SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950		

EXAMINER	
LANDSMAN, ROBERT S	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.



Art Unit: 1647

## **DETAILED ACTION**

### ***1. Formal Matters***

A. The Election filed 7/18/07 has been entered into the record. Applicants elected Group I without traverse. However, the Examiner noticed that the Lack of Unity mailed 6/22/07 inadvertently placed claims 24-26 into Group II instead of Group I. Therefore, claims 17-20, 22, 24-26 and 30-35 as drawn to elected SEQ ID NO:1, will be examined. Therefore, claims 17-35 are pending and claims 17-20, 22, 24-26 and 30-35 are the subject of this Office Action. The Restriction is deemed proper and is, therefore, made FINAL.

### ***2. Claim Objections***

A. Claim 33 is objected to since the term "cell derived" should be hyphenated.

B. Though none could be found, Applicant is advised that embedded hyperlinks and/or other forms of browser-executable code are impermissible and require deletion. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01(p), paragraph I regarding incorporation by reference.

C. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. The term "Hybond" appears on page 12, line 13.

D. Though none could be found, any U.S. or Foreign Applications cited in the specification which have since issued should be updated with the corresponding Patent No.

Art Unit: 1647

**3. Claim Rejections - 35 USC § 112, second paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 17-20, 22, 24-26 and 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: that the method be performed under conditions suitable for expression of the polypeptide

Claims 17-20, 22, 24-26 and 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention -

B. Claim 17 recites “production cycle.” However, a definition of this term could not be found in the specification.

C. Claims 20, 22 and 24-26 are rejected Claim 20 recites “active fraction.” It is unclear how this term relates to a protein. In other words, it is not understood to what a “fraction” of a protein refers. Claims 22 and 24-26 are rejected since they depend from claim 20.

D. Claims 20, 22 and 24-26 are confusing since it recites “circularly permuted derivative.” It is unclear how this term is defined. Claims 22 and 24-26 are rejected since they depend from claim 20.

**4. Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 17-20, 22, 24-26, 30 and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Browning et al. (WO 00/036092 – reference F1 on the 1449 filed 6/15/06). The claims recite a method of increasing recombinant protein production by culturing cells, including CHO cells, at temperatures

Art Unit: 1647

below 29 degrees C. The claims also recite the use of serum-free media and purifying the produced protein. Browning teach improving the production of recombinant proteins in CHO cells by lowering the cell culture temperature to between about 27 to about 35, preferably 27 to 32 degrees C (page 4-5; page 10, lines 20-22; Table II). Browning also teach purifying the protein (p5, line 29). Purified protein would inherently be “collected” as seen in claim 32. Claim 12 of Browning teaches pharmaceutical compositions. Though Browning do not specifically teach TBP-1, the instant claims recite fragments, or active fragments thereof. Since the TNF of Browning have at least one amino acid in common with that of TBP-1, Browning meet the limitations of “a fragment thereof.” The “active fragment” can be interpreted as a single amino acid with the activity of being able to be used in the production of a peptide.

### ***5. Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

A. Claims 18-20, 31 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Browning et al. (discussed above under 35 USC 102) in view of Nopar (1990 – reference R25 on the 1449 submitted 6/15/060. Claims 18-20 depend from claim 17, but recite the use of a TBP-1 polypeptide of SEQ ID NO:1. The teachings of Browning are taught above. Browning do teach expression of TNF receptors, but do not teach the use of the TNF Binding Protein, TBP-1. However, Nopar do teach the TBP-1 of SEQ ID NO:1 (see additionally page 6, lines 22-26 of the instant specification). Given the teachings of decreased temperature on the protein of Browning, it would have been obvious for one of ordinary skill in the art at the time of the present invention to have lowered the temperature in CHO cells regardless of the recombinant protein desired to be produced. The motivation can be seen on page 10 of Browning, which states –

Reducing the temperature during cell culture resulted in significantly less of the misfolded smaller form (i.e. the inactive form) being secreted. This improvement is presumably due to a reduced folding rate of the polypeptide which would allow for more time to fold the individual domains of the LTI~R portion prior to assembling the receptor-Ig fusion protein into the expected dimer form. The absolute temperature required to slow down the folding process is host dependent. For mammalian cells (i.e. CHO), the claimed method preferably occurs at temperatures of about 27°C to about 35 °C, more preferably, the temperature is about 27°C to about 32°C.

Art Unit: 1647

Therefore, it can be seen that, regardless of the protein, the ideal temperature for CHO cells to produce increased recombinant protein yield is 27 to 32 degrees. This decreased temperature leads to significantly less misfolded, inactive protein than does higher temperatures.

Under *KSR*, it's now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated. When there is motivation to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try may show that it was obvious under § 103 (*KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, \_\_\_, 82 USPQ2d 1385, 1397 (2007)).

## 6. Conclusion


A. No claim is allowable.

### *Advisory information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (571) 272-0888. The examiner can normally be reached on M-F 10 AM – 7 PM (eastern).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao at 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Robert Landsman, Ph.D.  
Primary Examiner  
Art Unit 1647